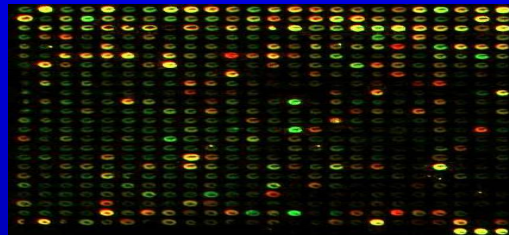


Genomics and Infectious Diseases: How Can We Integrate Genomics into Infectious Disease Research, Prevention, and Control?



Kumar V. Udhayakumar
Malaria Branch
Division of Parasitic Diseases
Coordinating Center for Infectious Diseases

Genomics and Public Health in the 21st Century

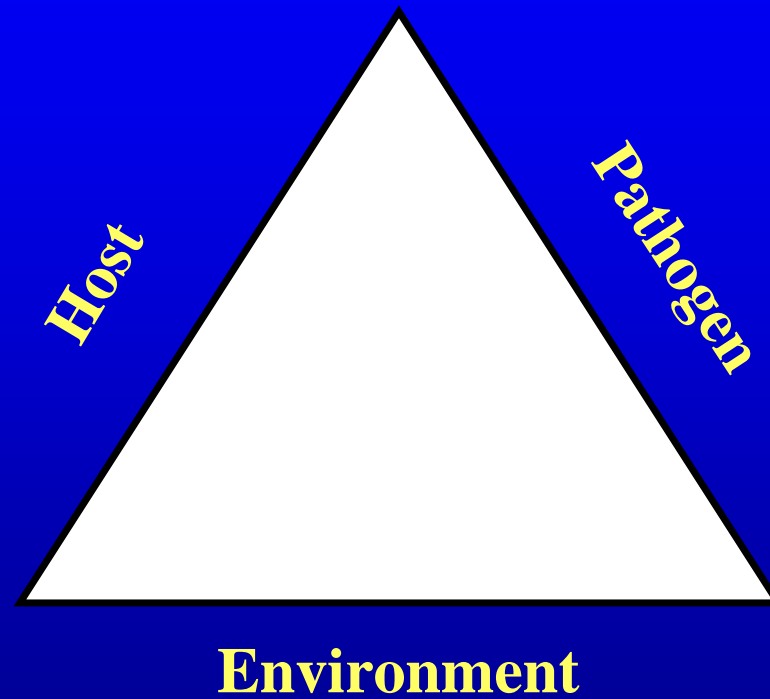
•“Genomics will be to the 21st century what infectious disease was to the 20th century...Genomics should be considered in every facet of public health: infectious disease, chronic disease, occupational health, environmental health, in addition to maternal and child health”

-Gerard et al. Journal Law, Medicine , Ethics 2002;

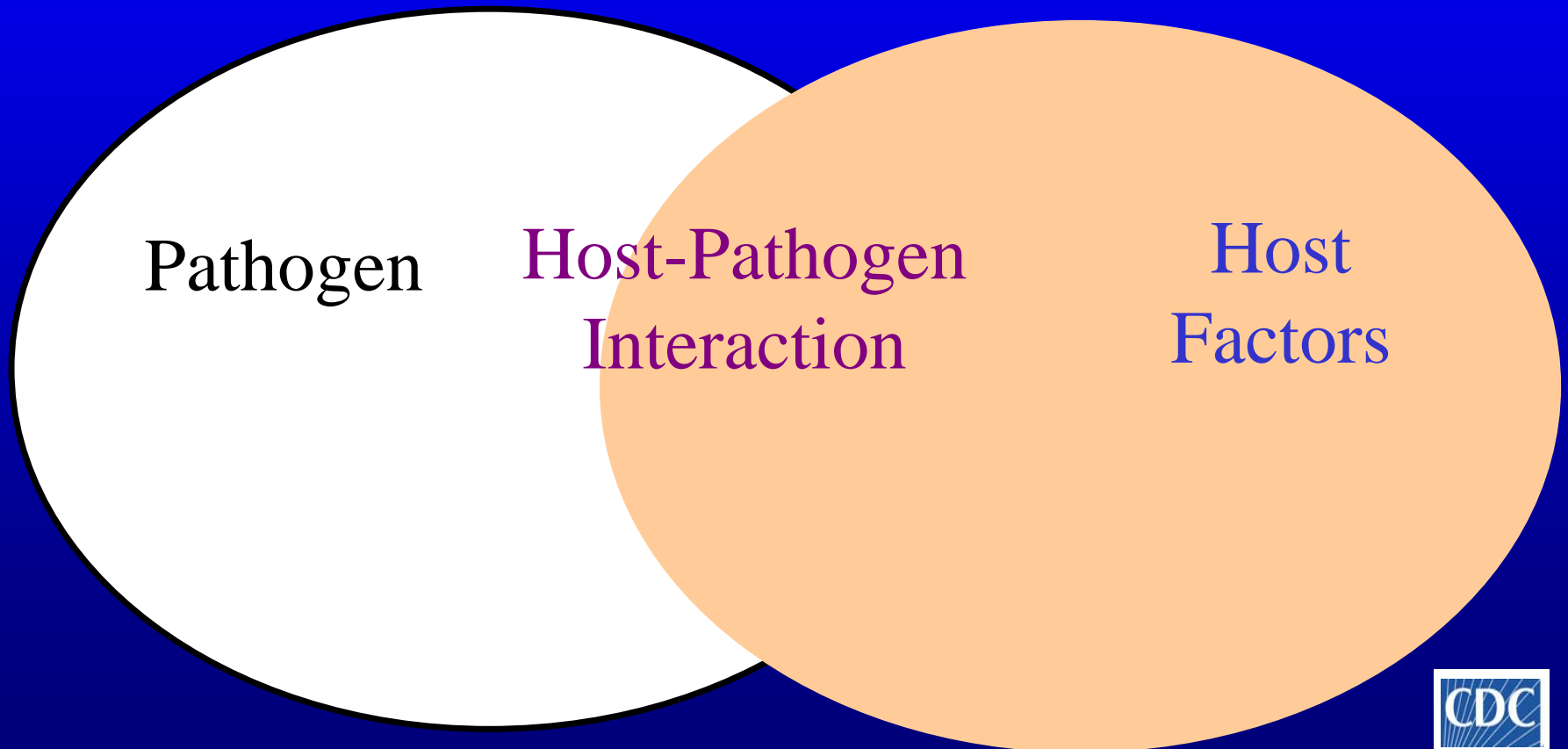
vol 30(suppl):173-176



Epidemiologic Triangle



Genomic tools are relevant for both sides of coin



Integrating Human Genomics into Public Health Use

- Genomics:
 - As diagnostic tool
 - As epidemiologic tool
 - To identify genetic risk factors/biomarkers
 - To target appropriate interventions
 - To determine drug/vaccine safety and responsiveness
 - To investigate bioterrorism

Genetic Clue Pursued in Families Struck by Bird Flu

By Alan Sipress

Washington Post Foreign Service

Wednesday, February 15, 2006; Page A14

BANDUNG, Indonesia -- Buenah's teenage daughter lay sprawled on a hospital bed, under observation for bird flu. In an adjacent room, her haggard husband was sitting wrapped in a gray blanket, also under treatment for the virus. Her two other children had already died from it.

“Buenah, who kept a vigil for her husband and daughter while they were in the hospital, has not shown symptoms of bird flu. She is the only one in her immediate family not to fall ill”.

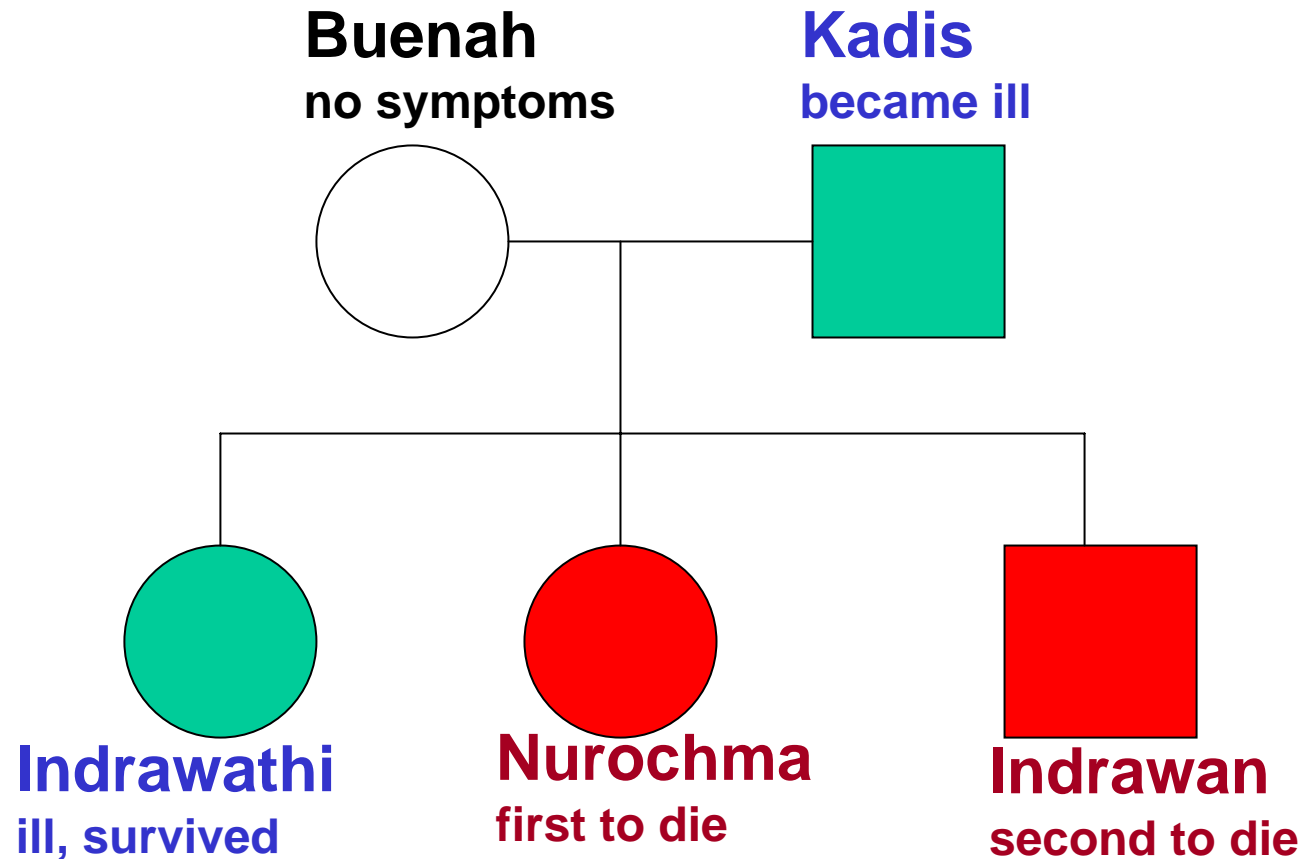
With four cases confirmed or suspected, her family represents one of the largest clusters of bird flu among humans in the world.Those infected by the virus were related to each other by blood and not by marriage. This raises the possibility that genetics play a role in determining who among those exposed contracts the often-lethal disease.

"It's intriguing," said Sonja J. Olsen of the Centers for Disease Control and Prevention in Bangkok,.....



Bird Flu Cluster

Is there a role for genetic risk factors?



With genomics tools it is possible to identify genetic risk factors

153 Child Deaths Linked to Flu During 2003-2004 Season.

Bhat et al.,

N Engl J Med. 2005 Dec 15;353(24):2559-67.

Is there a genetic basis?



**Why some people transmit
certain diseases better than
others (eg: SARS-super
spreaders)?**

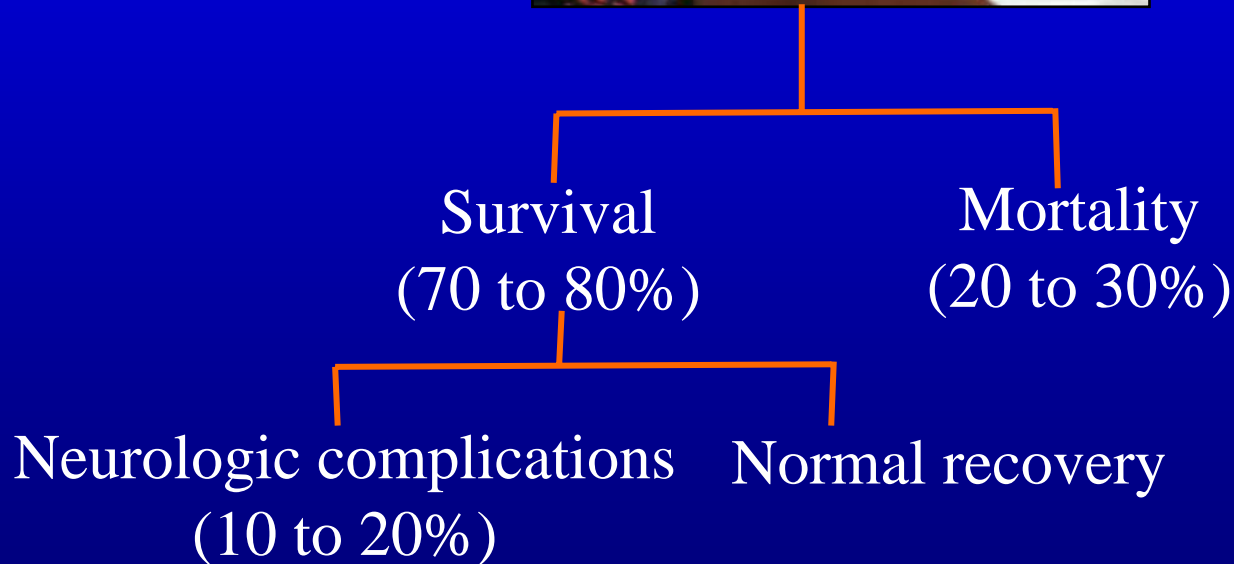
Is there a genetic basis?

Potential Identification of Prognostic Markers

Cerebral malaria-a major cause for mortality and morbidity



Pathogenesis?



Identification of a Prognostic Marker for SARS

Protein chip array profiling analysis in patients with SARS identified serum amyloid A protein as a biomarker potentially useful in monitoring the extent of pneumonia.

-YIP TT et al., Clin Chem. 2005 Jan;51(1):47-55

Genomic Tools for Hepatitis

- Over 2 billion people affected
- HBV- Over 350 million long-term carriers
- HCV- over 200 million infected- 80% carrier rate- many in developed countries.
- Use genomic tools for identification of prognostic markers for chronic carriers and to understand the biological basis for chronic infection

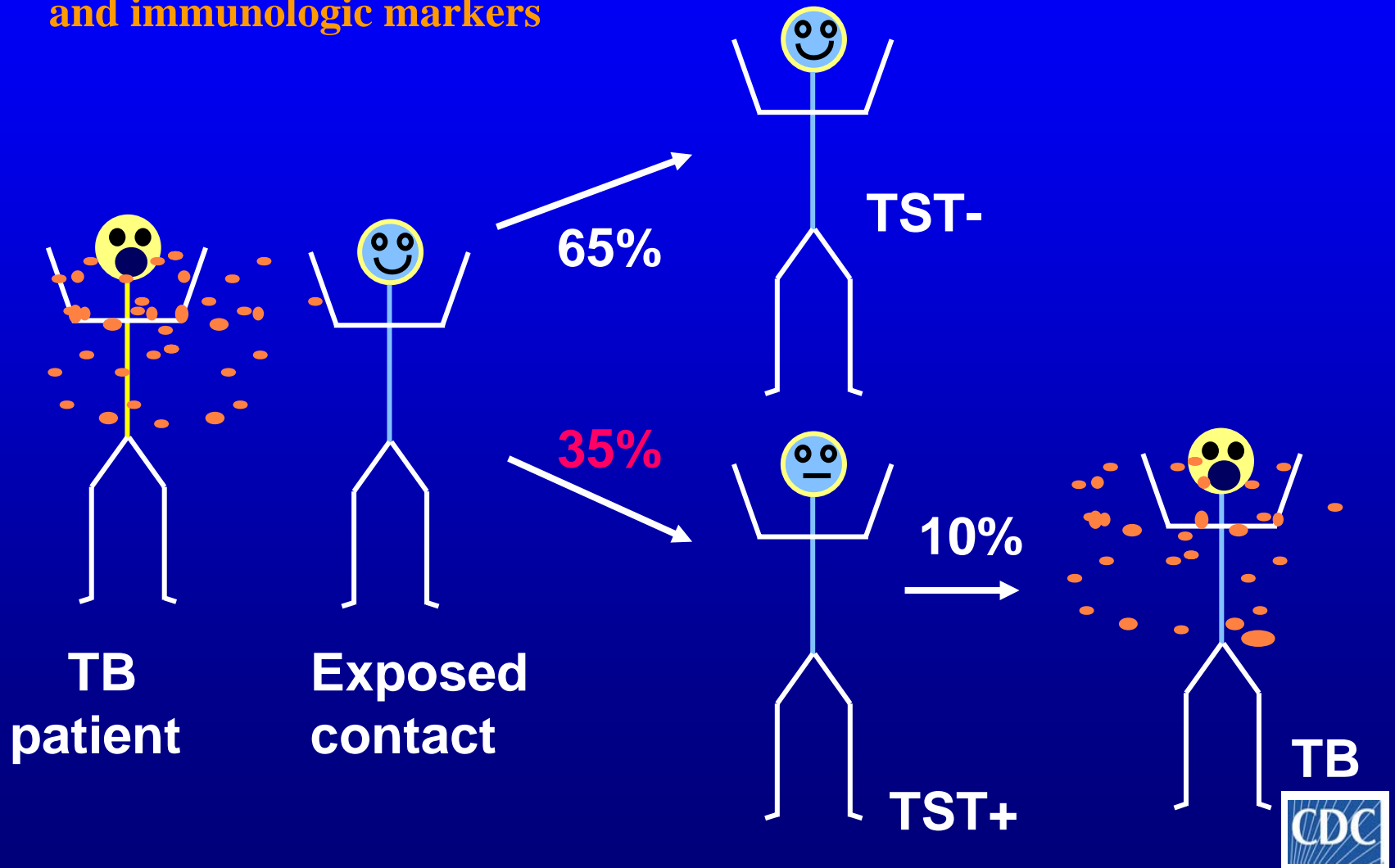
Genomic Tools for Hepatitis

- Low response rate to primary interferon-alpha therapy
 - HBV: 30 to 40%
 - HCV: <25%

Use genomics tools to identify responders and develop alternate treatment options for nonresponders.

Who is likely to develop tuberculosis?

Mary Reichler et al's study looks for genetic clues and immunologic markers



Immunization Safety in the Genomic Era

Current Research Underway

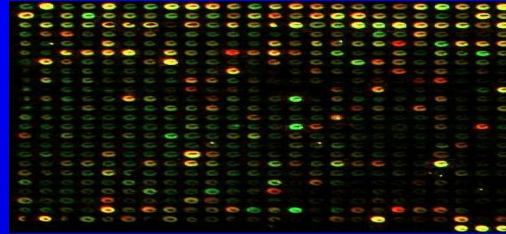
- **Smallpox Vaccination and Myopericarditis**
 - Case-control study using DoD vaccine recipients
- **Rheumatoid Arthritis and Hepatitis B vaccine**
 - Population based case ascertainment from Vaccine Safety Datalink
 - Case-only study of gene-vaccine interaction
- **Yellow Fever vaccine-associated viscerotropic disease (YEL-AVD)**
 - Case series study

Future research

- **Adverse event registry**
 - Generic registry of adverse events following immunization
 - Heterogeneous clinical data and biological specimens



Diagnostic/Epidemiologic Tool



- Multiple agents can be identified simultaneously
- Virulent factors can be identified
- Strain/source identification
- Anti-microbial resistance
- Disease specific host gene expression signatures
- Host-Pathogen interaction and chronic diseases

Some Examples

Genome-wide molecular dissection of serotype M3 group A Streptococcus strains causing two epidemics of invasive infections.

Stephen B. Beres et al., PNAS. 2004 Aug 10;101(32):11833-8.

Use of genome level-informed PCR as a new investigational approach for analysis of outbreak-associated Mycobacterium tuberculosis isolates.

Rajakumar et al., J Clin Microbiol. 2004 May; 42(5): 1890–1896

Gene expression profiling of dysplastic differentiation in cervical epithelial cells harboring human papillomavirus 16.

Ranamukhaarachchi DG et al., Genomics. 2005 Jun;85(6):727-38

Genome sequence and comparative microarray analysis of serotype M18 group A Streptococcus strains associated with acute rheumatic fever outbreaks.

Smoot JC et al., PNAS. 2002 April 2; 99(7): 4668–4673

Broad-range bacterial detection and the analysis of unexplained death and critical illness. Nikkari S et al., Emerg Infect Dis. 2002 Feb;8(2):188-94



Summary

- **Incorporate genomic tools for CDC outbreak/epi and field research investigations.**
- **Strengthen training, infrastructure and other resources for incorporating genomic tools for CDC scientists.**
- **This will help to meet CDC's public health goals in the 21st century.**

Acknowledgements

- Dr. Lyna Zhang
- COCID Genomics Working Group